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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/512,829	02/25/00	GARVEY	D

025270
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HM12/0914

EXAMINER	
RAO, D	
ART UNIT	**PAPER NUMBER**
1624	12

DATE MAILED: 09/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/512,829	Garvey et al.
Examiner	**Art Unit**
Deepak Rao	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 16, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *35-55, 59-61, 64, 66, 68, 71, 72, and 76-78* is/are pending in the application.

4a) Of the above, claim(s) *42-45* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *35-41, 46-55, 59-61, 64, 66, 68, 71, 72, and 76-78* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claims 35-55, 59-61, 64, 66, 68, 71-72 and 76-78 are pending in this application.

Election/Restriction

Applicant's election of Group IX, claims 35-55, 59-61, 64, 66, 68, 71-72 and 76-78 in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election of the species Lansoprazole as the proton pump inhibitor and S-nitrosoglutathione as the compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or EDRF, or is a substrate for nitric oxide synthase, in paper no. 10 is acknowledged.

The guidelines in MPEP § 803.02 provide that upon examination if prior art is found for the elected species, the examination will be limited to the elected species.

Content of MPEP § 803.02 is provided here for convenience:

> As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the non-elected species would be held withdrawn from further consideration. As in the prevailing practice, **a second action on the merits on the elected claims would be final**.

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

The elected species was found to be unpatentable, and therefore, the search was limited to the elected species and the claims are examined with respect to the elected species. The non elected species and the generic subject matter drawn to the non elected species is withdrawn from further consideration. Claims 42-45 are withdrawn from consideration as being drawn to non elected subject matter.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 47-49 and 59-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a gastrointestinal disorder, does not reasonably provide enablement for preventing the same. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The scope of the above method claims is not adequately enabled solely based on proton pump inhibitory activity provided in the specification. The instant claims are drawn to 'a method of .... **preventing** gastrointestinal disorders' and therefore, the instant claim language embraces disorders not only for the treatment, but for "prevention" which is not remotely enabled. The instant compounds are disclosed have proton pump inhibitory activity and it is recited that the instant compounds are useful in the "prevention" of gastrointestinal diseases for which applicants provide no competent evidence. "To prevent" actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. The only test example 4 in the specification provides assay measuring the gastric lesion activity, however, it is inconceivable as to how the claimed compositions, not only treat but also "prevent" a myriad of diseases with different etiologies. Further, there is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

2. Claim 64 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claim is drawn to a therapeutic method using a 'bismuth complex' that comprises a composition. First, it is unclear what is intended by this term (see the rejection under 35 U.S.C. 112, second paragraph). The specification fails to enable the preparation of the claimed 'complex'. The specification and the discussion of the preparation of proton pump inhibitors disclose the starting materials to prepare the compounds and therefore, the composition instantly claimed. However, there is no discussion regarding forming a 'bismuth complex' in the specification, nor there are any reaction schemes illustrating the same. Further, the only example tested uses lansoprazole and not the complex thereof, which is structurally very different from the instantly recited complex such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the claimed complex. In view of the lack of direction provided in the specification regarding the preparation of the claimed complex, the unpredictability of chemical reactions, the lack of working examples regarding the activity of such complexes, one of ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed complex.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 53, 64 and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. Claims 53 and 68 recite "a method for treating *Helicobacter pylori* comprising...", wherein, the term "*Helicobacter pylori*" is a type of bacteria. It is not clear if applicant intends to treat the bacteria itself as claimed or an infection or disease due to the *Helicobacter pylori* bacteria.

2. Claim 64 recites 'a bismuth complex comprising at least one composition of ...', however, it is not clear what is intended by this complex of a composition. A metal complex is generally indicative of an interconnected structure. There is no disclosure in the specification regarding such complexes.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 35-41, 46-55, 59-61, 64, 66, 68, 71-72 and 76-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over [Nohara et al., U.S. Patent No. 4,628,098 or Depui et al., WO 97/25064] in combination with Stamler et al., U.S. Patent No. 5,380,758* in view of Place, U.S. Patent No. 5,403,830*; Eek et al., U.S. Patent No. 5,629,305*; Moormann et al., U.S. Patent No. 5,945,425#.

Nohara et al. (US'098), teaches benzimidazole compounds including lansoprazole that are useful in treating gastrointestinal disorders, see formula (I) in the reference and the specific compound in claim 10. Also, Depui et al. (WO'064), teaches proton pump inhibitors useful in the treatment of gastrointestinal disorders and exemplifies lansoprazole (see page 10, second compound). WO'064 teaches the combination of the proton pump inhibitor with a NSAID, which NSAID's include selective COX-2 inhibitors and NO releasing NSAID's (see page 13, lines 1-2) and antacid formulations (see page 17, lines 7+), however, the reference does not exemplify a S-nitrosothiol. Stamler et al., US'758 in the analogous art teaches S-nitrosothiols including S-nitrosoglutathione (see col. 10, line 36) that have gastrointestinal therapeutic activity (see col. 9, lines 34-47). Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of the above references because he would have had the reasonable expectation that the composition comprising the individual compounds of the references would have the same therapeutic activity as taught for each of the compounds. [T]he idea of combining

the references flows logically from their having been individually taught in the prior art. *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Claim 51 specifically recites the use of a bismuth-containing reagent. Note that Place, US'830 teaches the use of bismuth-containing reagents in treating gastrointestinal disorders. Therefore, in view of the teachings of US'830, one of ordinary skill in the art at the time of the invention would have been motivated to modify the teachings of US'098 or WO'064 to include the bismuth-containing reagent in the composition because he would have had the reasonable expectation that the composition would have the same therapeutic activity as taught for the individual components.

Claim 53 and 68 are drawn to treating *Helicobacter pylori*. Note that Eek et al. US'305 teaches the treatment of gastritis, etc. and the infections caused by *Helicobacter pylori* using a proton pump inhibitor (e.g., lansoprazole) and an acid degradable antibacterial compound, see the abstract. Therefore, in view of the teaching of US'305, one of ordinary skill in the art would have been motivated to modify the teachings of [(US'098 or WO'064) and US'758] and use the combined composition as a therapeutic agent for treating infections due to *Helicobacter pylori*.

Claims 54-55 and 71 are drawn to a method of treatment of a viral infection. Note that Moormann et al. US'425 teaches treatment of viral infections using benzimidazole compounds that are (H+/K+)-ATPase inhibitors, see the reference. Therefore, in view of the teachings of US'830, one of ordinary skill in the art at the time of the invention would have been motivated to modify the teachings of [(US'098 or WO'064) and US'758] and use the combined composition

as a therapeutic agent for treating viral infections. Such modification would have been obvious because the skilled artisan would have expected the composition to having similar therapeutic application.

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* References cited in the specification.
# Reference cited in the IDS.

Duplicate Claims - Warning

1. Applicant is advised that should claims 47-49 be found allowable, claims 59-61 will be objected to under 37 CFR 1.75 as being a substantial duplicates thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

2. Applicant is advised that should claim 51 be found allowable, claim 64 will be objected to under 37 CFR 1.75 as being a substantial duplicates thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k)

3. Applicant is advised that should claim 52 be found allowable, claim 66 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing,

despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k)

4. Applicant is advised that should claim 53 be found allowable, claim 68 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

5. Applicant is advised that should claims 54-55 be found allowable, claims 71-72 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Receipt is acknowledged of the Information Disclosure Statement filed on April 11, 2000 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (703) 305-1879. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm. The fax phone number for

the organization where this application or proceeding is assigned is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Deepak Rao
September 13, 2001